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REMARKS/ARGUMENTS

Claims 29 through 45 are currently pending in the instant patent application. Applicants are herewith amending claims 29 and 34, and canceling claims 38 through 45. Claims 29 and 34 have been amended to include an additional step of "selecting dichloroacetic acid having a concentration of chloral hydrate less than 15ppm." These amendments are supported by the specification and claims as originally filed and therefore add no new matter to the instant patent application. With these amendments claims 29-37 remain pending in the instant patent application.

Rejections Under 35 U.S.C. §102(b) and/or §103(a) over Atkinson et al.

Claims 29-45 have been rejected in the Office Action as being anticipated by, or in the alternative, obvious over Atkinson et al. Applicants respectfully traverse.

The claims of the instant patent application are novel over Atkinson because: i) Atkinson does not teach the deprotection of a support-bound nucleotide with dichloroacetic acid having less than 15ppm chloral hydrate; and ii) Atkinson does not teach the step of selecting a dichloroacetic acid with a particular threshold concentration of chloral hydrate for use in the deprotection of a support-bound nucleotide.

The Office Action alleges that Atkinson inherently teaches the claimed invention in the instant patent application because Atkinson suggests the use of "HPLC grade" reagents during oligonucleotide synthesis. Applicants submit that the characterization of Atkinson is improper because Atkinson never identifies the chloral hydrate impurity as one to be avoided when selecting the grade of dichloroacetic acid used for deprotection of support-bound nucleotides. In addition, the Office Action assumes that producers and vendors of dichloroacetic acid purified their dichloroacetic acid so that levels of chloral hydrate were at or less than 0.0015%. Presently, high-grade dichloroacetic acid is sold by vendors, such as Sigma-Aldrich and J.T. Baker as a ≥99% pure solution, not identifying the percent level of chloral hydrate present. (*See* attached Exhibit A).

Although Applicants do not agree with the alleged rejection over Atkinson, independent claims 29 and 34 have been amended to include a step of "selecting dichloroacetic acid having a concentration of chloral hydrate less than 15ppm." This step of selecting dichloroacetic acid with 0.0015% or less chloral hydrate for use in deprotection of support-bound nucleotides is neither taught nor suggested in Atkinson. In addition, previously amended claims 36 and 37 also include steps of testing for and determining the amount of the choral hydrate impurity in a sample of dichloroacetic acid. These steps present in claims 36 and 37 are not taught nor suggested by Atkinson. Applicants therefore submit that the rejections under 102(b) and 103(a) are improper and should be withdrawn.

If the Examiner is of a contrary view, the Examiner is requested to contact the undersigned attorney at (760) 603-4631.

FEES

Fees associated with a three month extension of time are due to make the new due date August 14, 2006. A Petition for Extension of Time is attached hereto authorizing the Commissioner the appropriate amount to Isis Pharmaceuticals, Inc., Deposit Account Number 50-0252, referencing Attorney Docket No. ISIS-5245.

Respectfully submitted,

Date: August 14, 2006

Jason D. Ferrone, Esq.
Registration No. 52,887

Isis Pharmaceuticals, Inc.
1896 Rutherford Road
Carlsbad, CA 92008

P. 760.603.4631
F. 760.603.3820

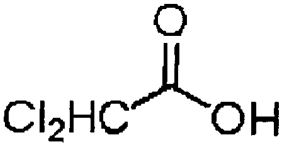
Exhibit A

©www.sigma-aldrich.com

Product Name or No. Go

D54702 Dichloroacetic acid

Sigma-Aldrich ***ReagentPlus*®, ≥99%**



Molecular Formula	$Cl_2CHCOOH$
Molecular Weight	128.94
CAS Number	79-43-6
Beilstein Registry Number	1098596
EG/EC Number	2012070
MDL number	MFCD00004223

Expand/Collapse All

Price and Availability

Click For Pricing and Availability

Descriptions

Packaging	1 kg in glass btl 5, 100, 500 g in glass btl
Legal Information	*ReagentPlus* is a registered trademark of Sigma-Aldrich Biotechnology.

Properties

grade	*ReagentPlus*®
vapor density	4.5 (vs air)
vapor pressure	0.19 mm Hg (20 °C)
assay	≥99%
refractive index	*n*20/D 1.466(lit.)
bp	194 °C(lit.)
mp	9-11 °C(lit.)
Fp	>230 °F >230 °F
density	1.563 g/mL at 25 °C(lit.)

References

Merck	*Merck* 13,3075
Beilstein	*Beil.* 2,IV,498
Fieser	*Fieser* 16,115
reference	*Aldrich MSDS* 1, 601:A / *Corp MSDS* 1 (1), 1109:A / *FT-IR* 2 (1), 790:D / *FT-IR* 1 (1), 508:B / *FT-NMR* 1 (1), 792:A / *IR-Spectra* (3), 298:C / *IR-Spectra* (2), 268:H / *NMR-Reference* 2 (1), 444:B / *RegBook* 1 (1), 555:H / *Sax* 6, 928 / *Sigma FT-IR* 1 (1), 1380:C / *Structure Index* 1, 79:C:1 / *Vapor Phase* 3, 591:C

Safety

Hazard Codes	C,N
Risk Statements	35-50
Safety Statements	26-45-61
RIDADR	UN 1764 8/PG 2
WGK Germany	2
RTECS	AG6125000

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... Routine Reagents > **Reagent Plus**

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Dichloroacetic Acid, BAKER ANALYZED Reagent

MSDS

Formula: **$Cl_2CHCOOH$**
Formula Weight: **128.94**

Product Number	Group Code	Units per Case	Pkg Size	Container Type	Unit Price	Case Price
G895-04	SPR	---	3 L	Glass	$ 853.75	N/A
G895-04	SPR	4	3 L	Glass	$ 569.15	$ 2276.60
G895-03	SPR	---	4 L	Glass	$ 1039.60	N/A
G895-03	SPR	4	4 L	Glass	$ 693.05	$ 2772.20

Actual Lot Analysis Reported on Label

Appearance	Passes Test
Assay ($Cl_2CHCOOH$) (by titration)	min. 99 %
Identification (by IR)	Passes Test
Refractive Index, n^{20}_D	1.46 - 1.47
Transmittance	

440 nm	Actual Value Reported
Water (H_2O)	Actual Value Reported

CAS Number: **79-43-6**
Merck Index: **13,3075**
IMO: **8:1764**
Specific Gravity: **1L = 1.56 Kg**
Spill Kit: **Acid Spill Cleanup**
Storage Color Code: **White**
Management of Change: **N**

Material Safety Data Sheet

	Health	Flammability	Reactivity	Contact
SAF-T-DATA Rating	1	0	1	3

Next

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